

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re            Reissue Application of Hashem Akhavan-Tafti  
                 Reissue of U.S. Patent 6,001,614  
                 Issue Date: December 14, 1999  
                 Applicant: Hashem Akhavan-Tafti

Box Reissue  
Commissioner of Patents and Trademarks  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT UNDER 37 CFR 1.115 AND STATEMENT OF  
STATUS AND SUPPORT FOR CHANGES TO THE CLAIMS**

Sir:

This amendment forms a part of the original application for reissue of U.S. Patent 6,001,614 filed concurrently herewith and is expressly incorporated by reference into the application. After according the application a filing date and prior to the first Office Action, please amend the claims as follows:

In the Claims:

Amend Claims 1 and 23. Add new Claims 24-29.

1. (Amended) A method comprising:

a) providing a reaction mixture comprising a single stranded nucleic acid template, a primer having at least 15 bases which is complementary to a portion of the single stranded nucleic acid template and a plurality of oligonucleotide 5'-monophosphates wherein each oligonucleotide 5'-monophosphate [consists of not more than] has up to about 10 bases and wherein each of the oligonucleotide 5'-monophosphates is labeled;

b) hybridizing the primer with the template under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to form a primer-template hybrid having a single stranded region and a double stranded region;

c) ligating more than one of the plurality of labeled oligonucleotide 5'-monophosphates in a contiguous manner onto the primer in one continuous process under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to extend the double stranded region and synthesize a labeled complementary nucleic acid strand, wherein ligation of oligonucleotide 5'-monophosphates only occurs in the presence of the hybridized primer.

23. (Amended) A method for synthesizing a labeled double stranded nucleic acid wherein both strands are labeled comprising:

- a) providing a reaction mixture comprising a double  
5 stranded nucleic acid template, a first primer which is complementary to a region of a first strand of the template, a second primer which is complementary to a region of a second strand of the template, wherein both primers have at least 15 bases, and a plurality of labeled oligonucleotide  
10 5'-monophosphates wherein each oligonucleotide 5'-monophosphate [consists of not more than] has up to about 10 bases and wherein each oligonucleotide 5'-monophosphate is labeled;
- b) separating the first and second strands of the double  
15 stranded nucleic acid;
- c) hybridizing the first and second primers with the separated strands under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to form first and  
20 second primer-template hybrids;
- d) ligating more than one of the plurality of labeled oligonucleotide 5'-monophosphates in a contiguous manner onto each primer-template hybrid in one continuous process under conditions which permit stable hybridization of the primer  
25 but not stable hybridization of the oligonucleotide 5'-monophosphates to extend the first and second primers thereby



24. (New) A method comprising:

5       a) providing a reaction mixture comprising a single  
stranded nucleic acid template, a primer which is  
complementary to a portion of the single stranded nucleic  
acid template and a plurality of oligonucleotide 5'-  
monophosphates, wherein the length of each of the  
oligonucleotide 5'-monophosphates is relatively short in  
comparison to length of the primer and wherein each of the  
oligonucleotide 5'-monophosphates is labeled;

10       b) hybridizing the primer with the template under  
conditions which permit stable hybridization of the primer  
but not stable hybridization of the oligonucleotide 5'-  
monophosphates to form a primer-template hybrid having a  
single stranded region and a double stranded region;

15       c) ligating more than one of the plurality of labeled  
oligonucleotide 5'-monophosphates in a contiguous manner onto  
the primer in one continuous process under conditions which  
permit stable hybridization of the primer but not stable  
hybridization of the oligonucleotide 5'-monophosphates to  
20       extend the double stranded region and synthesize a labeled  
complementary nucleic acid strand, wherein ligation of  
oligonucleotide 5'-monophosphates only occurs in the presence  
of the hybridized primer.



27. (New) A method for synthesizing a labeled double stranded nucleic acid wherein both strands are labeled comprising:

- a) providing a reaction mixture comprising a double stranded nucleic acid template, a first primer which is complementary to a region of a first strand of the template, a second primer which is complementary to a region of a second strand of the template, and a plurality of labeled oligonucleotide 5'-monophosphates wherein each oligonucleotide 5'-monophosphate is relatively short in comparison to length of the primers and wherein each oligonucleotide 5'-monophosphate is labeled;
- b) separating the first and second strands of the double stranded nucleic acid;
- c) hybridizing the first and second primers with the separated strands under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to form first and second primer-template hybrids;
- d) ligating more than one of the plurality of labeled oligonucleotide 5'-monophosphates in a contiguous manner onto each primer-template hybrid in one continuous process under conditions which permit stable hybridization of the primer but not stable hybridization of the oligonucleotide 5'-monophosphates to extend the first and second primers thereby producing double stranded nucleic acid, wherein ligation of oligonucleotide 5'-monophosphates only occurs in the presence

of the hybridized primer; and

e) repeating steps b-d at least once thereby  
synthesizing a labeled double stranded nucleic acid wherein  
both strands are labeled.

28. (New) The method claim 27 wherein each of the  
oligonucleotide 5'-monophosphates has up to about 10 bases.

29. (New) The method of claim 27 wherein each primers has at  
least 15 bases.

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## REMARKS

The present application is a reissue application of U.S. Patent 6,001,614 which issued on December 14, 1999 from U.S. Patent Application 09/241,353. Claims 1-29 are currently pending including claims 1-23 in the patent and newly added claims 24-29. Claims 1 and 23 have been amended.

### Statement of Support 37 CFR 1.173(c)

Independent claims 1 and 23 have been amended in regard to the definition of the size of the sets of oligonucleotide 5'-monophosphates. Applicant seeks to use the definition found in the specification at column 4, line 24-25. At the time the claims were amended during prosecution, under the law prevailing at that time, Applicant did not think that issuance of the claims in the form present in the '614 patent would result in a complete bar to covering the use of oligonucleotide 5'-monophosphates having more than 10 bases. This belief is reflected in a statement found in an amendment in the patent file styled "Second Supplemental Amendment Under 37 CFR §1.115"

"It is noted that the upper size of oligonucleotides claimed is 10 bases, the specification describes a size range of 2 to about 10. It is Applicant's position that the size difference between primer and oligonucleotide is more important. One of ordinary skill in the art will recognize the ability to make minor changes in the size of primers or oligonucleotides to be outside the precise size ranges stated in the

claims without departing from the meaning of the claims as long as a significant size difference is maintained between primer and oligonucleotide."

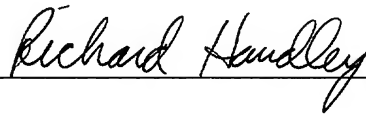
Recent changes in the law now call that belief into question. Applicants point out that it was not strictly necessary to include the limitation of "not more than 10 bases" or the "consisting" language to distinguish the claims from the prior art of record, particularly U.S. Patent 5,888,731 to Yager and U.S. Patent 5,403,708 to Brennan as applied by the Examiner. Applicant is not attempting to now claim subject matter which was given up during prosecution.

New claims 24-29 are directed to additional embodiments and rely on a concept not previously claimed but clearly disclosed in the specification at e.g. column 11, line 41 to column 12, line 6. Each of the new independent claims tracks the language of the original independent claims except with respect to the lengths of the primer and oligonucleotides. It is clear from this passage and the numerous worked examples that an essential feature of the methods is that there be a significant size difference, in base length, between primers and the oligonucleotide 5'-monophosphates. The new claims differ from the issued claims in specifying a length difference between the primers and the oligonucleotide 5'-monophosphate even though embodiments encompassing that length difference were claimed in the patent. Applicant

believes he erred in claiming less than what he had a right to claim by not presenting claims describing this essential relationship.

Because this is an application for a Reissue patent, all changes in the claims are indicated in the patent. Therefore, changes to the patent claims are not presented in the normal amendment style with both clean and marked-up versions of the amended claims. Applicants asked to be advised if the form of this amendment is improper.

It is believed that the Claims as presented are allowable. A first Office Action on the merits is respectfully requested.



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